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EXAMINER	
COTTON, ABIGAIL MANDA	
ART UNIT	**PAPER NUMBER**
1617	

DATE MAILED: 08/24/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/772,809	BERNSTEIN, JOEL E.	
	Examiner	Art Unit	
	Abigail M. Cotton	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 February 2006 and 28 June 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15* is/are pending in the application.

4a) Of the above claim(s) *1-8* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *9-15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-15 are pending in the application, with claims 1-8 having been withdrawn as drawn to non-elected inventions. Accordingly, claims 9-15 are being examined on the merits herein.

Applicant's arguments filed June 28, 2006 have been fully considered but they are not persuasive. Accordingly, the rejections of the claims are being maintained. The rejections of record are repeated below for Applicant's benefit.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 9-15 are rejected under 35 U.S.C. 102(b) as being anticipated by WO 98/50044 to Frank S. Caruso, published November 12, 1998.

Caruso teaches treating neuropathic pain with a composition having an antidepressant (see abstract, in particular.) Caruso teaches that the antidepressant can

be a tricyclic antidepressant such as imipramine hydrochloride, doxepin hydrochloride, among others (see page 4, lines 1-19, in particular.) Caruso teaches that an oral method of administration can be employed, and the composition may be provided as tablets or hard capsules, which are pharmaceutically acceptable vehicles (see page 6, lines 5-12, in particular.) Caruso furthermore teaches that the composition can have a non-narcotic analgesic such as acetaminophen or naproxen (see page 7, lines 10-24, in particular.) Caruso also teaches that the composition can be formulated to provide a desired dosage level of the components per day, and teaches formulating with pharmaceutically acceptable ingredients and excipients (carriers) (see page 5, lines 20-25 and page 6, lines 10-25, in particular.)

It is respectfully noted that for the purposes of searching for and applying prior art under 35 U.S.C. 102 and 103, the transitional phrase "consisting essentially of" is being construed as equivalent to "comprising." See, e.g., PPG, 156 F.3d at 1355, 48 USPQ2d at 1355, and MPEP 2111.03.

Regarding claims 9-15, Caruso teaches exemplary tablet dosage forms having antidepressant drugs and an additional active component that is a non-narcotic analgesic (see page 10, lines 5-37, in particular.) Regarding claims 11-12 and 14-15, Caruso teaches that the tablet form can comprise compositions with 25 mg of imipramine hydrochloride and 325 mg of aspirin or acetaminophen (see examples 36 and 37, in particular.) Thus, Caruso teaches the composition having the claimed

tricyclic antidepressant compounds and non-narcotic analgesics, and also teaches the claimed pharmaceutically acceptable vehicle.

Regarding claims 9-10, Caruso's teaching of 25 mg of imipramine hydrochloride in considered to meet the limitation of being a "low dose" of tricyclic antidepressant compound as claimed, because it falls within the range of "about 25 mg/day or less," in accordance with the definition of the "low dose" as set forth by Applicants in the first full paragraph on page 3 of the specification. Caruso's teaching thus also meets the limitation of being from "about" 2.5 mg to "about" 25 mg daily as recited in claim 10.

Regarding claims 9 and 13, Caruso's teaching of 325 mg of acetaminophen is considered to meet the limitation of being a "standard dose" of non-narcotic analgesic compound as claimed, because it falls within the range of "about 0.5 grams to about 2.6 grams," in accordance with the Applicants' guidance of a suitable "standard dose," which is set forth in the second full paragraph on page 3 of Applicants' specification. In particular, 325 mg of acetaminophen is considered to be within the range of "about" 0.5 grams to "about" 2.6 grams, as set forth by Applicants.

Accordingly, the tablet dosage forms taught by Caruso anticipate the compositions of claims 9-15.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 9-12 and 14-15 are rejected under 35 U.S.C. 103(a) as being obvious over U.S. Patent No. 4,579,846 to Crawford et al, issued April 1, 1986, in view of U.S. Patent No. 4,434,164 to Joseph G. Lombardino, issued February 28, 1984.

Crawford et al. teaches an anti-inflammatory composition for the treatment of gastric irritation that employs the anti-inflammatory piroxicam (a non-steroidal anti-inflammatory drug) with the antidepressant doxepin (a tricyclic anti-depressant) (see abstract and column 3, lines 45-58, in particular.) Crawford et al. teaches that the piroxicam can be provide in a range of 0.1 to 1 mg/kg/day, whereas the second ingredient, such as doxepin, can be provided separately in an amount that is generally lower than the dosages typically specified in the prior art (see column 3, lines 45-55, in particular.) Crawford et al. also teaches that in a combined formulation, the proportion of each drug is the ratio of the total daily dosage of each drug when dosed alone (see column 3, lines 55-68, in particular.) That is, Crawford et al. teaches that the combined formulation could comprise the (i) 0.1 mg/kg/day dose of piroxicam with (ii) the lower

dose of doxepin that is taught by Crawford et al. as being provided if the drugs are administered alone (i.e. not in combination, separately.) Crawford et al. also exemplifies a treatment composition comprising 20 mg of piroxicam and 20 mg doxepin with lactose and hydroxypropyl methylcellulose (carriers), and teaches that a dosage of the piroxicam can be from 5-50 mg/day (see Example 9 and column 4, lines 1-10, in particular.)

It is respectfully noted that for the purposes of searching for and applying prior art under 35 U.S.C. 102 and 103, the transitional phrase "consisting essentially of" is being construed as equivalent to "comprising." See, e.g., PPG, 156 F.3d at 1355, 48 USPQ2d at 1355, and MPEP 2111.03.

Crawford et al. does not specifically teach that the compositions as exemplified comprise a "standard dose" of a non-narcotic analgesic and a low dose of a tricyclic antidepressant, as recited in claim 9.

Lombardino teaches novel salts of piroxicam that provide anti-inflammatory activity (see column 1 line 1 through column 2 line 60, in particular.) Lombardino teaches that a suitable dose of the piroxicam salt can be from 5 mg up to 1000 mg per day (see column 3, liens 18-25, in particular.)

Accordingly, Crawford et al's dosage of 5 to 50 mg/day (see column 4, lines 1-10, in particular), falls within the dosage range as taught by Lombardino et al. to be useful for anti-inflammatory action, and thus is considered to be a "standard dose" of piroxicam. Accordingly, it is considered that one of ordinary skill in the art at the time the invention was made would have found it obvious to provide the "standard" normal dose of piroxicam as taught by Crawford et al. and Lombardino, with a lower dose of doxepin, as taught by Crawford et al, with the expectation of providing a suitable anti-inflammatory composition for the treatment of gastric irritation.

Regarding claim 10, Crawford et al. teaches that the dosage of doxepin can be from 4 to 200 mg/day (see column4, lines 5-10, in particular), and exemplifies a composition with 20 mg, and thus meets the limitation of the claim. Furthermore, it is considered that one of ordinary skill in the art at the time the invention was made would have found it obvious to vary and/or optimize the amount of doxepin provided in the composition, according to the guidance provided by Crawford et al, to provide a composition having desired anti-inflammatory properties. It is noted that "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955.)

Regarding claim 11, Crawford et al. teaches providing doxepin, as recited in the claim. Regarding claim 12, Crawford et al. teaches that doxepin is marketed in the form

of its hydrochloride salt (see column 3, lines 15-20, in particular), and thus it would be obvious to one of ordinary skill in the art to provide doxepin hydrochloride because Crawford et al. teaches that this is a doxepin form that available on the market. Regarding claim 14, Crawford et al. teaches providing piroxicam, which is a non-steroidal anti-inflammatory. Regarding claim 15, Crawford et al. teaches that the composition can be provided as a tablet or capsule (see column 4, lines 15-20, in particular.)

Response to Arguments

Applicant's arguments filed June 28, 2006 have been fully considered but they are not persuasive.

Regarding Applicant's argument that the composition is consisting essentially of, rather than comprising, the claimed components, it is noted that the transitional phrase "consisting essentially of" is being construed as equivalent to "comprising" for the purposes of searching for and applying prior art under 35 U.S.C. 102 and 103, as discussed above. See, e.g., PPG, 156 F.3d at 1355, 48 USPQ2d at 1355, and MPEP 2111.03. Applicants argue that the term "consisting essentially of" excludes elements from the claimed combination that have essential significance, and the included elements must not materially affect the basis and novel characteristics of the claimed invention. However, Applicant's have not disclosed what components are considered to

be of "essential significance", and thus are to be excluded from the composition. What components do not materially affect the basis characteristics of the composition, and thus are considered to be encompassed by the composition, and which components are to be understood to be excluded? As no such explanation has been provided in the application as filed, the transitional phrase "consisting essentially of" is being construed as equivalent to "comprising" for the purposes of searching for and applying prior art under 35 U.S.C. 102 and 103, as discussed above.

Applicants further argue that there is no motivation to combine Crawford and Lombardino because Lombardino is not analogous art. Lombardino is directed to salts of piroxicam useful as pharmaceutical agents, and thus is considered to provide teachings in the pharmaceutical arts, and thus shares analogous subject matter both with the pharmaceutical compositions of Crawford et al. as well as the instantly claimed treatment compositions.

Applicants further provide analysis of each reference individually with comments and an analysis of the relationship between each reference and the instantly claimed invention, in the table spanning pages 5-6 of the instant application. In response to applicant's arguments against the references individually, the Examiner notes that one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208

USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Applicants argue that Lombardino merely teaches novel crystalline salts. The Examiner notes that Lombardino is being applied in combination with Crawford et al. to show the claimed treatment composition is obvious.

Applicants also argue that Caruso teaches that the antidepressants must be provided in an "amount sufficient to alleviate neuropathic pain," and refers to the dosages specified in Goodman and Gilman, which include dosages of antidepressants of from 75-30 mg daily. However, the Examiner notes that, as discussed above, Caruso exemplifies compositions having dosages of the antidepressant and analgesic that meet the limitations of being a "low dose" and a "high dose" as recited in the claim, and thus the compositions as taught by Caruso meet the limitations of the claims.

Applicants also argue that Caruso specifies a combination of antidepressant and NMDA receptor antagonist, and teaches that a large number of other actives can be provided, and thus Applicants imply that Caruso does not teach the composition "consisting essentially of" the components. However, as discussed above, the transitional phrase "consisting essentially of" is being interpreted as being equivalent to "comprising" for the purposes of searching and applying prior art, and thus the teachings of Caruso are considered to meet the limitations of the claims.

Applicants argue that Crawford does not teach providing the combination of tricyclic antidepressant and non-narcotic analgesic for the treatment of pain. It is respectfully pointed out that the recitation that the composition is "for treatment of chronic pain" in claim 1 has not been given patentable weight because the recitation occurs in the preamble. A preamble is generally not accorded any patentable weight where it merely recites the purpose of a process or the intended use of a structure, and where the body of the claim does not depend on the preamble for completeness but, instead, the process steps or structural limitations are able to stand alone. See *in re Hirao*, 535 F.2d 67, 190 USPQ 15 (CCPA 1976) and Kropa v. Robie, 187 F.2d 150, 152 88 USPQ 478, 481 (CCPA 1951.)

Applicants further argue that Crawford teaches a dosage of doxepin (antidepressant) of from 3.3 to 33 mg/kg (see Table I), and argues that this translates into a dosage of 248-2480 mg for women and 287-2870 mg per day for men, which is much higher than the "lower dose" of from 2.5 to 25 mg as recited for example in claim 10. The Examiner notes that Table I teaches dosages for rats, not humans. Furthermore, Crawford specifically teaches that a suitable oral dosage of doxepin can be from 4 to 200 mg/day (see column 4, lines 1-10, in particular), as discussed above, which overlaps with the recited "low dose." Furthermore, it is considered that one of ordinary skill in the art at the time the invention was made would have found it obvious to vary and/or optimize the amount of doxepin provided in the composition, according to the guidance provided by Crawford, to provide a composition having desired properties.

It is noted that "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955.)

Conclusion

No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Abigail M. Cotton whose telephone number is (571) 272-8779. The examiner can normally be reached on 9:30-6:00, M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

AMC

SREENI PADMANABHAN
SUPERVISORY PATENT EXAMINER